

REMARKS

Claims 21-32 are pending in the instant application. A complete list of the pending claims is presented above. Reconsideration of the claims in light of the following remarks is respectfully requested. No new matter is included in the amendments presented above.

Priority

The Examiner has objected to the specification on the grounds that the instant invention does not include a claim of priority as the first sentence of the application. In light of the amendment to specification, presented above, Applicants respectfully request withdrawal of this objection.

Specification

The Examiner has objected to the drawings on the grounds that the figures include Figures 1A to 1H, 2A-1 to 2A-9 and 2B-1 to 2B-9, however the Brief Description of the Drawings only refers to Figures 1 and 2. In light of the amendment to the specification, presented above, Applicants respectfully request withdrawal of this objection.

Claim Objections

The Examiner has objected to Claims 25 and 30 on the grounds that the reference to “ruthenium” should properly be to “a ruthenium atom.” Similarly, the Examiner has objected to Claims 26 and 31 on the grounds that the reference to “iron” should properly be to “an iron atom.” In light of the amendments to the claims, presented above, Applicants respectfully request withdrawal of this objection.

Claim Rejections

A. 35 U.S.C. § 102(b)

Claims 21-23 and 27-29 stand rejected under 35 U.S.C. § 102(b) as anticipated by Inoue et al, U.S. Patent No 4,965,350 (“Inoue”). In particular, the Examiner asserts that Examples 1-3 (columns 13-16), which describe the production of 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl) 2, 7-dioxypyrido[2, 3-d]pyrimidine, teaches a nucleotide having three phosphates and a hydroxyl group on the 2' position of its ribose, and asserts that the supposed 2' hydroxyl group acts as a covalently attached ETM.

Claim 21 is an independent claim directed to a composition comprising a modified nucleotide triphosphate further comprising a covalently attached ETM. Claims 22 and 23 depend from Claim 21 and specify, respectively, that the ETM is attached to the ribose, or that ETM attached to the 2' carbon of the ribose. Claim 27 discloses a method of employing the composition of Claim 21 in the production of a nucleic acid. Claims 28 and 29 further define the method as employing the compositions of Claims 22 and 23.

For an anticipation rejection under 35 U.S.C. §102(b) to be proper, a single reference must expressly or inherently disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)).

As pointed out above, the Examiner has cited 3-(5'-O-triphosphoryl-beta-D-deoxyribofuranosyl) 2, 7-dioxypyrido[2, 3-d]pyrimidine as teaching a nucleotide having three phosphates and a hydroxyl group on the 2' position of its ribose. However, contrary to the assertion by the Examiner, the cited compound does not have the claimed 2' hydroxyl. This is clear not only from the name of the compound ('**deoxyribofuranosyl**') but also by review of the

cited Examples. For instance, in Example 3 the compound is labeled “d” and contains no hydroxyl on the 2’ carbon of the ribose. See Column 16, Lines 15-30. Thus, the Examiner has not pointed to any disclosure in Inoue that teaches nucleotide triphosphates having an attached ETM as is currently claimed in either the composition claims (Claims 21-23) or the method claims (Claims 27-29). As the Examiner has not carried his burden under §102(b), Applicants respectfully request for withdrawal of the rejection.

Claims 21, 22, 24, 25, 27, 28, 30 and 31 stand rejected under 35 U.S.C. § 102(e) as anticipated by Bannwarth et al., U.S. Patent No 5,278,043 (“Bannwarth”). In particular, the Examiner asserts that the ruthenium complex depicted in Figure 6 is an ETM and thus compound depicted in Figure 1 (ruthenium complex H-phosphonate covalently attached to the 5’ carbon of guanine) is a modified nucleotide triphosphate comprising an attached ETM.

As discussed above, Claim 21 is directed to a composition comprising a modified nucleotide triphosphate further comprising an attached ETM. Claims 22, 24 and 25 depend from Claim 21 and specify that the attached ETM is attached to the ribose (Claim 22); is a transition metal complex (Claim 24); or is a ruthenium complex (Claim 25). As is also described above, Claim 27 discloses a method of employing the composition of Claim 21 in the production of a nucleic acid. Claims 28, 30 and 31 further specify that that the ETM attached to the nucleotide triphosphate: is attached to the ribose (Claim 28); is a transition metal complex (Claim 30); or is a ruthenium complex (Claim 31).

For an anticipation rejection under 35 U.S.C. §102(e) to be proper, a single reference must expressly or inherently disclose each and every element of a claim. *In re Paulsen*, 31

USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)).

As a preliminary matter, Applicants traverse the Examiners interpretation of the phrase “modified nucleotide triphosphate” as including modified nucleotide monophosphates, such as the modified nucleotide monophosphate described in Bannwarth. Such a definition completely ignores the Applicant’s consistent use of the phrase in the specification, for example, at page 21, line 29, to page 22, line 6:

The amino-modified nucleotides made as described above are converted to the 2’ or 3’ modified nucleotide triphosphate form using standard biochemical methods (Fraser et al., Proc. Natl. Acad. Sci. USA, 4:2671 (1973)). One or more modified nucleosides are then attached at the 3’ end using standard molecular biology techniques such as with the use of the enzyme DNA polymerase I or terminal deoxynucleotidyltransferase (Ratliff, Terminal deoxynucleotidyltransferase. In The Enzymes, Vol 14A. P.D. Boyer ed. pp 105-118. Academic Press, San Diego, CA. 1981).

This passage clearly articulates that the claimed “modified nucleotide triphosphate” refers to a modified nucleotide having three phosphate moieties. It is well established that a patentee may be her own lexicographer. *Chef America Inc. v. Lamb-Weston Inc.*, 69 USPQ2d 1857, 1860 (CA FC 2004). Accordingly, Applicants respectfully request that the Examiner withdraw his interpretation of “modified nucleotide triphosphate” as including modified nucleotides having other than three phosphate moieties. One of skill in the art would not interpret a “modified triphosphate” as including a mono- or di- phosphate.

The Examiner’s basic position appears to be that covalent attachment to a phosphate of a nucleic acid is a covalent attachment to the ribose of the nucleic acid. This interpretation is clearly not supported by the specification, which distinguishes between covalent attachment to the ribose, phosphate backbone and the base. Thus, the Examiner’s interpretation of the term

“covalently attached” clearly exceeds the use of the term found in the specification, for example at page 32, line 25 to page 33, line 2:

In accordance with a further aspect of the invention, the preferred formulations for donors and acceptors will possess a transition metal covalently attached to a series of ligands and further covalently attached to an amine group as part of the ribose ring (2' or 3' position) or to a nitrogen or sulfur atom as part of a nucleotide dimer linked by a peptide bond, phosphoramidate bond, phosphorothioate bond, phosphorodithioate bond or O-methyl phosphoramidate bond.

This passage differentiates between covalent attachment at the 2' position and covalent attachment at the 3' position of a ribose, which would not exist under the Examiner's interpretation. As is pointed out above, it is well established that a patentee may be her own lexicographer. *Id.* Accordingly, Applicants respectfully request that the Examiner withdraw his overly broad interpretation of “covalent attachment.”

Furthermore, in contrast to the Examiner's assertion, Bannwarth et al. does not teach electron transfer, but rather, “energy transfer” systems; see for example column 2, lines 28-36:

These energy-transfer systems can also, in the wider sense, be defined as donor-acceptor energy transfer systems. The donor component is to be understood to mean, in general, those compounds which are able to absorb light from an energy source and then release it to an acceptor. By acceptor is generally meant those compounds which are able to absorb this energy release by the donor.

Such energy transfer is completely different from the present invention, which involves electron transfer. Thus, the Examiner's statement that Bannwarth discloses electron acceptors and electron donors is incorrect. As the Examiner has not pointed to any disclosure in Bannwarth teaching a modified nucleotide triphosphate further comprising a covalently attached ETM, the Examiner has not carried his burden under 35 U.S.C. §102(e), and withdrawal of the rejection is respectfully requested.

B. 35 U.S.C. § 103(a)

Claims 26 and 32 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Bannwarth. In particular, the Examiner asserts that it would have been prima facie obvious to substitute iron for ruthenium as “the replacement would not change the intended use of the transition metal complex.” See 12/23/03 Office Action, Page 7.

To establish a prima facie case of obviousness the prior art reference must teach or suggest all the claim limitations. In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) M.P.E.P. §2143.

As discussed above, Bannwarth does not teach or suggest the use of modified nucleotide triphosphates as required by Claims 26 and 32. Furthermore, Bannwarth does not teach electron transfer moieties also required by Claims 26 and 32. Accordingly, the Examiner has not carried his burden in establishing a prima facie case of obviousness and therefore Applicants respectfully request withdrawal of the 305 U.S.C. § 103(a) rejection.

C. Double Patenting

Claims 21-24 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,780,234. Although Applicants do not accede to the Examiner’s assertion that Claims 21-24 of the instant application are unpatentable over Claims 1-12 of U.S. Patent No. 5,780,234, in the interest of expediting prosecution, a terminal disclaimer directed to U.S. Patent No. 5,780,234 is enclosed.

Claims 21-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,591,578. Although

Applicants do not accede to the Examiner's assertion that Claims 21-26 of the instant application are unpatentable over claims 1-8 of U.S. Patent No. 5,591,578, in the interest of expediting prosecution, a terminal disclaimer directed to U.S. Patent No. 5,591,578 is enclosed.

Claims 21-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of U.S. Patent No. 6,087,100. Although Applicants do not accede to the Examiner's assertion that Claims 21-26 of the instant application are unpatentable over claims 1-16 of U.S. Patent No. 6,087,100, in the interest of expediting prosecution, a terminal disclaimer directed to U.S. Patent No. 6,087,100 is enclosed.

Claims 21-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 6,238,870B1. Although Applicants do not accede to the Examiner's assertion that Claims 21-26 of the instant application are unpatentable over claims 1-12 of U.S. Patent No. 6,238,870B1, in the interest of expediting prosecution, a terminal disclaimer directed to U.S. Patent No. 6,238,870B1 is enclosed.

Claims 21-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18 of U.S. Patent No. 6,177,250B1. Although Applicants do not accede to the Examiner's assertion that Claims 21-26 of the instant application are unpatentable over claims 1-18 of U.S. Patent No. 6,177,250B1, in the interest of expediting prosecution, a terminal disclaimer directed to U.S. Patent No. 6,177,250B1 is enclosed.

Claims 21-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3-13 of U.S. Patent No. 5,770,369. Although Applicants do not accede to the Examiner's assertion that Claims 21-26 of the instant application are unpatentable over claims 1 and 3-13 of U.S. Patent No. 5,770,369, in the interest of expediting prosecution, a terminal disclaimer directed to U.S. Patent No. 5,770,369 is enclosed.

Claims 21-26 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-12 of U.S. Patent No. 5,705,348. Although Applicants do not accede to the Examiner's assertion that Claims 21-26 of the instant application are unpatentable over claims 1-12 of U.S. Patent No. 5,705,348, in the interest of expediting prosecution, a terminal disclaimer directed to U.S. Patent No. 5,705,348 is enclosed.

Claims 21 and 22 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 6,063,573 ("the '573 patent"). Claims 1-11 of the '573 are directed to compositions comprising a primary single-stranded scissile probe comprising a nucleic acid having both a first portion comprised of DNA, a second portion comprised of RNA, and a third portion comprised of DNA. Applicants note that the claim does not specify that the 5' end of the primary single-stranded scissile probe is a nucleotide triphosphate, and that this fact is assumed by the Examiner. However, in order to include the claimed DNA and RNA subunits, the probe would have to be artificially synthesized rather than enzymatically synthesized. As artificial synthesis of nucleic acids uses

phosphoramidite chemistry instead of the triphosphate hydrolysis of enzymatic synthesis, the Examiner's assumption that the 5' end would comprise a nucleotide triphosphate is incorrect. As claims 1-11 of the '573 patent are not directed to the same subject matter and do not fall within the scope of Claims 21 and 22 of the instant application, withdrawal of the double patenting rejection is respectfully requested.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance and early notification to that effect is respectfully requested. Please direct any calls in connection with this application to the undersigned attorney at (415) 781-1989.

Respectfully submitted,

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Dated: _____

By:



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